Accelerated Pathways for Emergency Vaccines and Other Vaccines of Public Health Importance

William M. Egan, Ph.D.

Acting Director

Office of Vaccines Research and Review

Center for Biologics Evaluation and Research, FDA

The Need for Accelerated Pathways

- Emerging and re-emerging diseases (*e.g.,* SARS)
- Bio-terrorism agents (*e.g.,* smallpox, anthrax)
- Vaccine shortages (*e.g.,* PCV-7, influenza)
- New vaccines of public health importance for the U.S. (*e.g.,* HPV, HIV)
- New vaccines of global public health importance (*e.g.,* TB, malaria, HIV, HPV, rotavirus)
- Pandemic strains of influenza virus

Vaccine Licensure

- The development of a vaccine is a complex process resulting in the licensure and commercialization of a product that has been *demonstrated to be safe and effective* and that *can be manufactured in a consistent manner*.
- The FDA is committed to fostering the efficient, rapid development of vaccines needed for the public health.

Vaccine Development

Pre IND

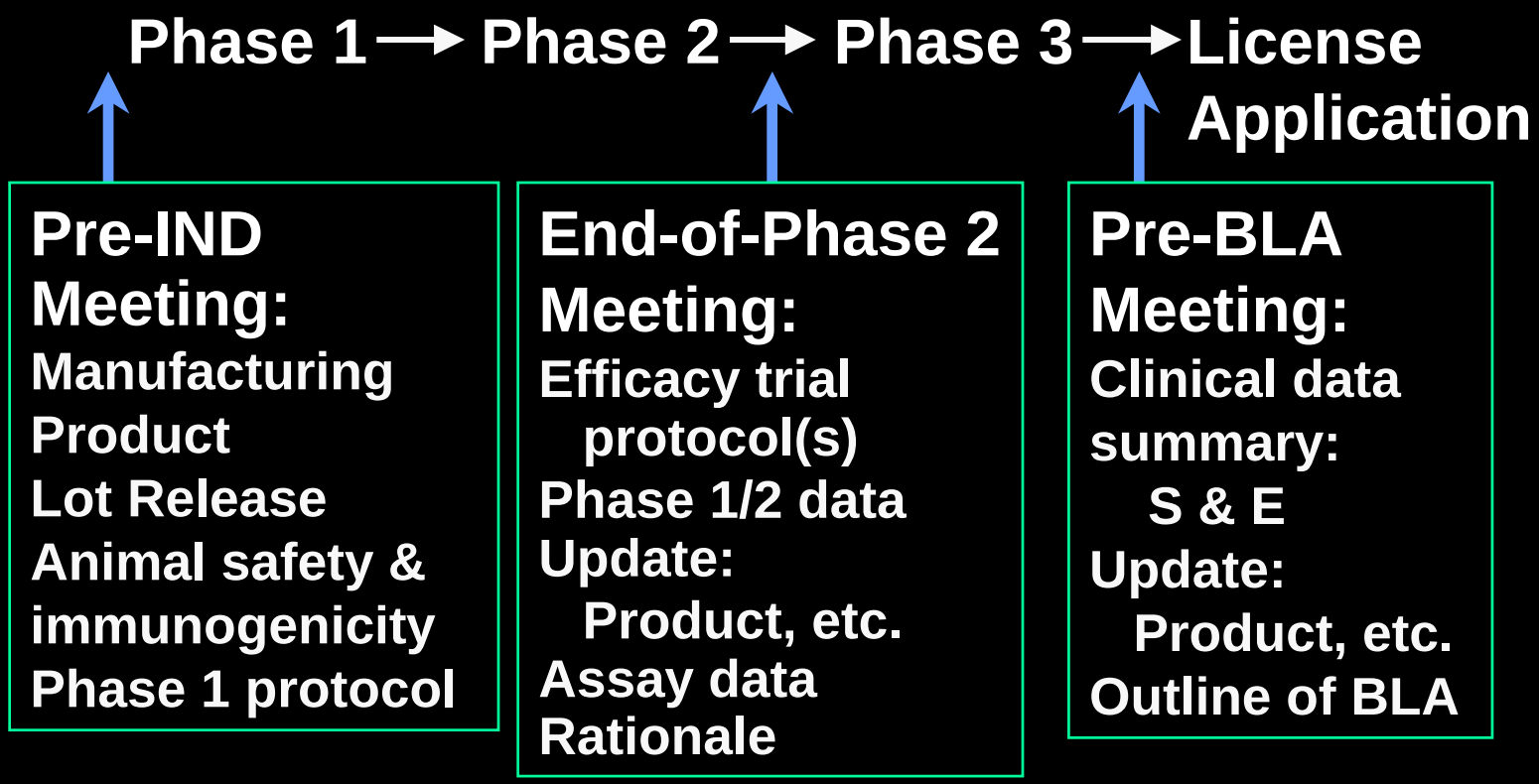
- Development of Rationale Based on Disease Pathogenesis
- Immunogen Identification
- Development of Manufacturing Process; Non-clinical Studies

IND

- Clinical Studies; Additional Non-clinical Work; Scale-up

IND =Investigational New Drug application

Meetings with FDA
(21 CFR 312.47)



IND =Investigational New Drug Application
BLA =Biologics License Application

Considerations for Vaccine Type: Viral Vaccine as an Example

- Live attenuated
  - Sufficiently attenuated? How to determine?
  - Potential for reversion? Markers for reversion?
  - Potential for transmission? Consequences of potential transmission in various populations?
- Inactivated
  - Adequacy of inactivation process (assays)
  - Are critical protective antigens/epitopes preserved (assays)?
  - Are potentially deleterious neo-antigens created?

Considerations for Vaccine Type: Viral vaccine (cont'd)

- Subunit, recombinant
  - Have the critical protective antigens been included and presented in a manner that induces protective immunity.
- Nucleic acid-based vaccine
  - Distribution and integration of the vector
  - Persistence of the vector
- Other issues
  - Adjuvants
  - Manufacturing residuals

Viral Vaccine Production

- Source and quality of starting materials
- Characterization of cell substrate: identity, history, endogenous retroviruses, adventitious agents (including potential TSE agents), tumorgenicity (if appropriate)
- Characterization of viral seed: identity, history, adventitious agents
- Validation of manufacturing process for removal or inactivation of viruses (depending on vaccine type)
- In process testing
- Release testing of bulk and final products: purity, potency, safety

Expediting the Review Process: Formal Mechanisms

- Fast Track
- Priority Review
- Accelerated Approval
- Guidance for Industry: Fast Track Drug Development Programs – Designation, Development, and Application Review (September, 1998)
  - http://www.fda.gov/cber/guidelines.htm

Fast Track Drug Development

- Designed to facilitate the development and expedite the review of new drugs that are intended to treat *serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs*.
- Intended to meet the need of Section 112(b) of the Food and Drug Administration Modernization Act of 1997.

Fast Track

- Incorporates an end of Phase I meeting
- Allows for a priority review of the BLA; allows for a “rolling” review of the BLA
- Allows for an accelerated approval of the product

Accelerated Approval

- Approval based on a determination that the effect of a surrogate endpoint is reasonably likely to predict clinical benefit (21 CFR 314.510 & 601.41)
- Post-licensure studies required
- Potential problems obtaining subsequent controlled clinical data

Priority Review

- 6 Month review of the entire BLA
- The review clock will not begin until the applicant has informed FDA that a complete BLA has been submitted
- Recent example is the pneumococcal conjugate vaccine, Prevnar.

The Challenge of Bioterrorism: an Innovative Approach to Regulation

- *New Drug and Biological Drug Products: Evidence Needed to Demonstrate Effectiveness of New Drugs when Human Efficacy Studies are not Ethical or Practical*. (The "Animal" Rule)
- For new drug and biological products that are intended to treat or prevent life-threatening or serious conditions.
- Use of animal efficacy data for approval

The Challenge of Bioterrorism: the Animal Rule

- Will not apply if approval can be based on standards described elsewhere (surrogate markers or clinical endpoints other than survival or irreversible morbidity.
- Safety evaluation of products is not addressed by this rule (i.e., human safety studies needed).
- Approval subject to post-marketing studies

Bioshield Legislation

- Legislation passed by the House and the Senate
- Provides for an Emergency Use Authorization
  - Emergency declared by Secretary of Homeland Defense or Secretary of Defense
  - EUA granted by Secretary of HHS
- Products known and potential benefits must outweigh the known and potential risks.

Bioshield Legislation (cont'd)

- The product's use and distribution may be limited
- The authorization will be time-limited and can be terminated

Pandemic Influenza

- Use existing mechanisms for current licensed influenza vaccines
- Pre-determine dosage and schedule
  - One dose or more needed
  - 15 µg or more (?)
  - Use of adjuvants
- Carry out studies with a strain to which the population is naïve (such as H5)

Speeding Product Development

- Early and frequent consultation between sponsor and FDA (improves quality and efficiency/reduces misunderstandings and potential for multiple cycles of review
- Formal mechanisms
  - Fast track
  - Accelerated approval
  - Priority review
- Approval under the “animal” rule
- Attention to risk:benefit and risk management issues

The Fundamental Challenge

Regulations and the applications of regulations are dependent on the existing level of science that will support a given action. The challenge for us all is to identify the gaps in our knowledge (the barriers that exist), to identify the pathways to addressing those gaps, and to define the criteria for acceptability.